Errata Page

AVAILABLE FOR PUBLIC DISCLOSURE WITHOUT REDACTION

1. At the time of submission of the briefing book, mortality rates associated with the Saltz irinotecan/5-FU/LV regimen had been obtained from four post-registration studies. Data have now become available from a 5th study, and we are presenting an update of the information as errata page. Updated figures in tables are shown with an underline.

In "Executive Summary"

Page iv: Table – Post-registration experience for the Saltz regimen to be updated to include 5 studies instead of 4 studies:

Regimen	Drugs	Studies	N	60-Day, All-Cause Mortality, %	
				Rate	95%CI
Post-registration Experience					
Saltz	Irinotecan/5-FU/LV	5 studies*	702	3.8	1.3- 6.2
Douillard	Irinotecan/5-FU/LV	4 studies	191	2.6	0.0- 6.9

* Includes NCCTG Study N9741

Page v: Paragraph 1, line 8: Update number of patients from post-registration experience with Saltz regimen from "436" to "702".

Page v: Paragraph 1, line 10: Update all-cause mortality rate from post-registration experience with Saltz regimen from "4.3% (95% CI: 1.5-7.0)" to "3.8% (95% CI: 1.3-6.2)".

In "Review of Mortality Rates in the Therapy of Colorectal Cancer"

Page 15: Last paragraph, line 4: Update number of patients for the Saltz regimen from "436" to "927"

Page 16: Display 7: Irinotecan/5-FU/LV section to be updated to include data from a 5th post-registration study (Genentech, Anti-VEGF 2001):

Regimen Sponsor [Author (Study) Year]	N	60-Day, All-Cause Mortality		Therapy-Related Mortality (Investigator Assessment)	
		Rate, %	95% CI, %	Rate, %	95% CI, %
Irinotecan/5-FU/LV					
Saltz Irinotecan/Bolus 5-FU/LV					
Post-registration	**702**	**3.8**	**1.3- 6.2**		
Aventis [Graeven 2000]	46	0.0	0.0- 7.7	0.0	0.0- 7.7
NCCTG [N9741 2001]	289	4.8	2.7- 8.0	NR	NA
Aventis [Ben Ayed 2001]	51	7.2	2.2-18.9	3.9	0.5-13.5
Sugen [SU5416-035 2001]	50	2.0	0.1-10.6	0.0	0.0- 7.1
Genentech [Anti-VEGF 2001]	266	3.0	1.3- 5.8	NR	NA
Pharmacia (Study 0038)	***225***	***6.7***	***3.8-10.8***	0.9	0.1- 3.2
Overall	**927**	**4.5**	**1.8- 7.2**		
Douillard Irinotecan/Infusional 5-FU/LV					
Post-registration‡	**191**	**2.6**	**0.0- 6.9**		
Aventis [Labianca 2001]	50	2.0	0.1-10.6	0.0	0.0 -7.1
Aventis [HK1.602 2001]	66	1.5	0.0- 8.2	0.0	0.0 -5.4
Aventis [Ben Ayed 2001]	53	3.8	0.5-13.0	1.9	0.0-10.1
Sugen [SU5416-035 2001]	22	4.5	0.1-22.8	4.5	0.0-22.8
Aventis (Study V303)	***145***	***2.1***	***0.4- 5.9***	0.7	0.0- 3.8
Overall‡	**336**	**2.4**	**0.0-5.5**		

Summary estimates (including 95%CIs) are computed using weighted averages of the individual study estimates and their standard deviations. Exact 95%CI were computed for the individual studies.
‡ Includes patients treated with irinotecan/5-FU/LV alone and with anti-VEGF antibody/irinotecan/5-FU/LV
Abbreviations: 5-FU = 5-fluorouracil, CI = confidence interval, ECOG = Eastern Cooperative Oncology Group, GITSG = Gastrointestinal Tumor Study Group, LV = leucovorin, NA = not applicable, NCCTG = North Central Cancer Treatment Group, NR = not reported, SWOG = Southwest Oncology Group

Page 17: Paragraph 3, line 4: Update 60-day post-registration mortality experience with the Saltz regimen from "4.3% (95% CI: 1.4-7.0%)" to "3.8% (95% CI: 1.3-6.2%).

2. We were informed on November 14, 2001 of an additional death on Study C89803, which results in the following updates:

Page iii: Update the number of deaths in 635 patients on C89803 from 15 (2.4%) to 16 (2.5%).

Page 12: Paragraph 2: At the end of the paragraph, delete "from a myocardial infarction" and add the following sentences:

> Since that time it has been identified by the CALGB that 2 additional patients on the irinotecan/5-FU/LV arm had died, 1 on Day 22 of therapy (May 8, 2001) and 1 on Day 93 of therapy (May 30, 2001). An additional patient on the 5-FU/LV arm died on Day 48 (June 10, 2001). Thus the Total 60-day, all cause mortality rate on Study C89803 was 16 of 635 patients (2.5%) among those patients treated with Saltz irinotecan/5-FU/LV and 6 of 628 patients (1.0%) treated with Roswell Park 5-FU/LV [L. Saltz – personal communication, November 14, 2001].

Page 18: Display 8: Update the table for the additional death as follows:

Regimen Sponsor [Author (Study) Year]	N	60-Day, All-Cause Mortality	
		Rate, %	95% CI, %
5-FU/LV			
Roswell Park Bolus 5-FU/LV			
NSABP [Wolmark 1999]	691	0.56 *	0.16-1.48
ECOG [Haller 1998]	946	0.85	0.37-1.66
CALGB [C89803 2001]	628	0.96	0.35-2.07
Overall	**2265**	**0.75**	0.14-1.35
Irinotecan/5-FU/LV			
Saltz Irinotecan/Bolus 5-FU/LV			
CALGB [C89803 2001]	635	2.52	1.45-4.06

3. In addition to the updates, the errata page contains some corrections:

Page 15: Last paragraph, line 5: Correct number of patients for the Douillard regimen from "191" to "336"

Page 44 (Appendix A) -Table 5: Correct levels of LDH as follows:

Adverse Event	Study 0038			Study V303			
	Irinotecan 5-FU/LV	5-FU/LV	Irinotecan	Irinotecan 5-FU/LV		5-FU/LV	
	Saltz Arm B N = 225	Mayo Clinic Arm C N = 219	Irinotecan Alone Arm A N = 223	Arm A N = 199		Arm B N = 186	
				AIO Arm A1 N=54	Douillard Arm A2 N=145	AIO Arm B1 N=43	deGramont Arm B2 N=143
Laboratory Abnormalities (%)							
LDH >ULN	60.3	55.5	53.3	42.8		45.2	

4. Other minor corrections:

Page ii: Table - Row 8: Correct "Regimens" to "Regimen"
Page ii: Table - Row 10: Add "Irinotecan/5-FU/LV Infusional Regimens"
Page 17: Paragraph 2, line 1: Correct "multicenter study " to "large study".
Page 17: Paragraph 3, lines 3 & 5: Correct "overall post-registration mortality experience" to "60-day post-registration mortality experience".
Page 42: (Appendix A) Table 3: Correct the number of patients in AIO arm A1 from "54" to "53".

Population	Study 0038			Study V303			
	Irinotecan 5-FU/LV	5-FU/LV	Irinotecan	Irinotecan 5-FU/LV		5-FU/LV	
	Saltz Arm B	Mayo Clinic Arm C	Irinotecan Alone Arm A	Arm A		Arm B	
				AIO Arm A1	Douillard Arm A2	AIO Arm B1	deGramont Arm B2
As-randomized (n)	231*	226*	226	199		188	
				53	146	45	143